REMARKS/ARGUMENTS

Claims Rejection - 35 USC § 112:

Independent claims 1 and 13 have been amended in the manner suggested by the Examiner to show the structure of the pyrone and thereby enable one to appreciate the chemical structure without reference to the drawing of the structure in the specification. Dependent claims 2 through 6 have been amended (claims 3-6 in the manner suggested by the Examiner) for clarity. As amended, claims 1 and 13, and claims 2-6 and 11-16 that depend therefrom, comply with the requirements of 35 USC § 112, second paragraph. The Examiner's courtesy in suggesting clarifying language is acknowledged with appreciation.

Independent claims 1 and 13 have also been amended to more particularly point out and distinctly claim the subject matter that applicant regards as his invention over the prior art cited by the Examiner.

Claims Rejection - 35 USC §§ 102 and 103:

Independent claims 1 and 13, as amended, are not anticipated or rendered obvious by Cherksey (US 5,234,947), Umbdenstock (US 5,332,579), or other cited prior art.

The Group of Compounds Claimed by Applicant Are Distinct from Those Described and Claimed By Cherksey

Applicant has amended claims 1 and 13 to eliminate the reference to R3 being an alkyl radical having 1 to 4 carbon atoms. As amended, the group of compound described in independent claims 1 and 13 are all the kavapyrones and are entirely distinct from the group of compounds described and claimed by Cherksey.

Cherksey describes a group of organic compounds having a chemical structure that is similar, but patentably distinct from, the group of compounds described and claimed by

Applicant. The R' group of Cherksey corresponds to the R3 position of the kavapyarone compounds claimed by Applicant. In the compounds of Cherksey, R' is a hyrdogen, lower alkyl, lower alkenyl or arakyl group. In the kavapyrones claimed by Applicant, R3 is either a styryl or phenethyl radical. None of the compounds described and claimed by Cherksey exhibit an aromatic ring group at position 3 (R'), whereas all the kavapyrones claimed by Applicant do.

While Cherksey makes vague references to kavapyrones, he discusses only one, kawain. Cherksey characterizes kawain as a potassium channel activating substance (col. 6 lines 63-64) without any supporting evidence, references or data. The study and data included in the Cherksey disclosure does not pertain to kawain or any other kavapyrone. The putative study was done on avena pyrone, a pyrone derived from oats, not a kavapyrone derived from the kava plant.

There is also no literature support for the proposition that any kavapyrone is a potassium channel activator. Cherksey recognizes this when he states that it is not known that kavapyrones are postassium channel activators (col. 7 lines 2-4). Accordingly, Cherksey's statement that kawain is a potassium channel activator is left unsubstantiated.

Cherksey goes on to state that "[i]t has unexpectedly been found that the substitution of a lower alkyl group for the more bulky aromatic group enhances the potassium channel activation effects of the compounds" (Col. 6 lines 65-68.) There are no kavapyrones wherein the a lower alkyl group is substituted for the aromatic group found at R3. All kavapyrones (see Applicant's specification, at pages 6-7) have an aromatic group at R3.

By altering the one kavapyrone described in Cherksey, and by structurally excluding all kavapyrones by substituting a lower alkyl group for the bulky aromatic ring group in position R3, Cherksey teaches away for the invention described and claimed by Applicant.

Claim 1 Recites a New and Unobvious Use for a Known Composition of Matter

The Examiner cites to *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978) and *In re Tomlinson*, 373 F.2d 928, 934, 150 USPQ 623, 628 (CCPA 1966) for the

proposition that the discovery of a new use for an old product/composition is finding a property in the old composition/product, and to *Altas Powder Co. V. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, '947 (Fed. Cir. 1999) and *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977) for the proposition that claiming a new use, new function or unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. Applicant respectfully submits that these cases are inapposite.

Claim 1, Applicant's independent method claim, claims a "new use of a known composition of matter" within the meaning of 35 U.S.C. § 100(b). Applicant has not claimed as novel and unobvious a property or characteristic that is inherent in a known composition of matter. Applicant is claiming that the discovery of a property or characteristic that is inherent to kavapyrones makes kavapyrones useful as an anti-craving agent in the treatment of alcoholics. It is the new use, not the newly discovered property or characteristic, that forms the patentable subject matter of Applicant's independent method claim. Cherksey, Umberstock, and the other prior art citations, neither described nor appreciated that kavapyrones inhered the property or characteristic that makes them useful as an anti-craving agent in the treatment of alcoholics.

Cherksey does not anticipate or make obvious kavapyones' usefulness as an anti-craving agent in the treatment of alcoholism. The reference relied upon in Cherksey (col. 4, lines 46-53) refers only to the "compounds of the present invention," being those that have "potassium channel activation properties," and then only as useful for the treatment of "withdrawal symptoms" from various substance addictions. Because Cherksey modifies the kavapyrones by substituting, at R3, simple hydrocarbon groups for the bulky aromatic ring groups, the kavapyrones of Applicant's invention are not anticipated by the compounds of the invention of Cherksey.

Moreover, use of a substance in the treatment of withdrawal symptoms from a substance addiction does not anticipate, nor does it render obvious, use of the same or similar substance to counteract the sensation of craving experienced by substance addicts. One skilled in the art of

addictions would not equate withdrawal symptoms and craving, nor would one skilled in the art of addictions assume a drug that effectively treats one would be effective for the other.

Alcohol withdrawal symptoms are a result of specific biochemical changes in the brain due to chronic exposure to alcohol. The biochemical basis of alcohol withdrawal symptoms is well described by Bayard M, McIntyre J, Hill KR, Woodside J Jr., *Alcohol withdrawal syndrome.* Am Fam Physician. 2004 Mar 15;69(6):1443-50, as follows:

> Alcohol withdrawal syndrome is mediated by a variety of mechanisms. The brain maintains neurochemical balance through inhibitory and excitatory neurotransmitters. The main inhibitory neurotransmitter is gamma-aminobutyric acid (GABA), which acts through the GABA-alpha (GABA-A) neuroreceptor. One of the major excitatory neurotransmitters is glutamate, which acts through the N-methyl-D-aspartate (NMDA) neuroreceptor.
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> Alcohol enhances the effect of GABA on GABA-A neuroreceptors, resulting in decreased overall brain excitability. Chronic exposure to alcohol results in a compensatory decrease of GABA-A neuroreceptor response to GABA, evidenced by increasing tolerance of the effects of alcohol.
>
> Alcohol inhibits NMDA neuroreceptors, and chronic alcohol exposure results in up-regulation of these receptors. Abrupt cessation of alcohol exposure results in brain hyperexcitability, because receptors previously inhibited by alcohol are no longer inhibited. Brain hyperexcitability manifests clinically as anxiety, irritability, agitation, and tremors. Severe manifestations include alcohol withdrawal seizures and delirium tremens.

Bayard et al (a copy of which is enclosed with this response) provides, in Table 2, a comprehensive listing alcohol withdrawal symptoms. Craving is not among the listed symptoms.

Williams D, Lewis J, McBride A., *A comparison of rating scales for the alcohol-withdrawal syndrome,* Alcohol and Alcoholism, 2001 Mar-Apr;36(2):104-8 (a copy of which is also enclosed with this responded) comprises a literature review of studies that evaluated alcohol withdrawal symptoms and rating scales. This exhaustive review considers all varieties of withdrawal symptoms. Craving is not among the withdrawal symptoms listed by any of the literature reviewed.

O'Brien CP, Childress AR, Ehrman R, Robbins SJ., *Conditioning factors in drug abuse: can they explain compulsion?*, J. Psychopharmacol. 1998;12(1):15-22, define craving as the primary motivating factor in drug use and the appropriate target of behavioral interventions. Robinson TE, Berridge KC, *The neural basis of drug craving: an incentive-sensitization theory of addiction,* Brain Res Brain Res Rev. 1993 Sep-Dec;18(3):247-91, refer to craving and relapse as the defining characteristics of addictions. They state that drug craving is fundamental to addiction. Addicts develop an obsessive craving for drugs so irresistible that it almost inevitably leads to drug seeking and drug taking. Singleton EG, Gorelick DA, *Mechanisms of alcohol craving and their clinical implications*, Recent Dev Alcohol. 1998;14:177-95 define craving as an outcome measure with craving reduction interpreted as treatment success.

Craving is distinct from withdrawal in the science of addiction. Craving is why an addict continues to be an addict. Without craving, there is no addiction. Craving is the definition of being an addict. Addicts do not have withdrawal symptoms, they only have craving. An alcoholic may or may not have withdrawal symptoms when he or she has stopped drinking, but the alcoholic will have craving for alcohol both before and after he or she has stopped drinking. This craving is unrelated to withdrawal symptoms.

An anti-craving agent is designed to treat the addict while the addict is still drinking so the addict can stop drinking and is no longer driven by craving to drink. The addict may then develop withdrawal symptoms, but such withdrawal symptoms are not related in any way to craving. The goal is to provide the alcoholic who wants to quit an anti-craving agent that will cause the addict's desire to drink to cease. Treating withdrawal symptoms does not treat the addition and does not assist the addict to stop drinking. Treating withdrawal symptoms only addresses the physical discomfort that sometimes accompanies the cessation of drinking.

Craving and withdrawal have a different biochemistry and a different locus of operation in the brain. Because craving is different from withdrawal symptoms, craving is graded by different scales. Four self-rating instruments for craving are: the Obsessive-Compulsive Drinking

Scale ("OCDS"), the Lubeck Craving Scale, the Alcohol Craving Questionnaire, and ordinal scales.

The OCDS is a 14 item self-rated questionnaire (enclosed). It measures the level of thoughts about alcohol, distress associated with those thoughts, resistance to those thoughts, and compulsive alcohol drinking behavior, distress associated with that behavior and resistance to that behavior. The OCDS measures a dimension of alcohol craving and operationalizes this concept. The questionnaire takes about 5 minutes to complete and be administered periodically at various time intervals to assess changes in the degree of craving, and thus addiction, over time. A review of the OCDS that is used to rate the level and intensity of craving is entirely different from, and is unrelated to, the withdrawal rating scales described in the literature reviewed by Williams et al., *supra*.

Withdrawal symptoms are well defined physical symptoms that have a well understood brain biochemistry. While the biochemistry of craving is less understood, much is now known with the advent of new scanning technology. The location of craving in the brain involves the dopaminergic neurons of the nucleus accumbens in the mesocorticolimbic reward system. Craving and withdrawal symptoms have different biochemistry and different locus of operation in the brain.

Craving and withdrawal symptoms have different methods of assessment, different biochemistry and a different locations in the brain. Craving leads to addiction while withdrawal symptoms are the result of addiction. Drugs and methodologies used to treat craving are typically different from drugs and methodologies used to treat withdrawal. A drug claiming patentability for the treatment of withdrawal symptoms would presumably have no applicability for the treatment of craving. And, in any case, the "obviousness to try" test is not the appropriate test to determining anticipation and obviousness in the context of specific compositions and methods developed by inventors. *In re Tomlinson*, 373 F.2d 928, 931, 150 USPQ 623, ___ (CCPA 1966).

The arguments and authority submitted by Applicant in its February 18, 2004 amendment and response as respects Umbdenstock (US 5,332,579) are repeated and incorporated herein by this reference.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." TEMP § 2131 at 2100-69 (8th Ed. 2001), *quoting Verdegaal Bros. v. Union Oil Co. Of California,* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir, 1987). Neither Cherksey nor Umbdenstock describe, expressly or inherently, compounds having the structural formula describes in independent claims 1 and 13, as amended, as an anti-craving agent in the treatment of alcohol addiction. Nor would it have been obvious in light of the disclosures of Cherksey or Umbenstock that the group of compounds known as kavapyrones would be useful as an anti-craving agent in the treatment of alcohol addiction.

Claim 13 Includes a Limitation Neither Anticipated nor Made Obvious by The Cited Prior Art

Independent claim 13 includes, as a limitation, a non-alcoholic beverage formulated to simulate the taste and aroma of an alcoholic beverage. None of the cited prior art include this limitation, expressly or by implication. Nor would this limitation have been obvious to one skilled in the pertinent art.

Other Matters

"If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious". MPEP § 2143.03 at 2100-126, *citing In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Accordingly, all dependent claims currently pending in this application are similarly new and unobvious.

Applicant has considered the other citation (Houdi) made of record and does not deem it material to the issue of patentability of the claimed invention.

In addition to the literature references stated to be enclosed herewith, Applicant is enclosing a complete copy of the *Coffey* article referenced in Applicant's February 18, 2004 amendment and response that the Examiner stated was not available in the file.

CONCLUSION

Applicant has offered amendments to claims 1 and 13 with clarifying language to overcome the Examiner's Section 112 rejection and to further distinguish the claimed invention over the cited art. Applicant is presenting evidence and argument establishing that amended claims 1 and 13 describe subject matter that is both new and unobvious, and should be allowed. As dependent claims 2 through 6 and 10 through 12 include all limitations found in independent claim 1, and dependent claims 14 through 16 include all limitations found in independent claim 13, the pending dependent claims should likewise be allowed. Accordingly, Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

The Examiner is invited to contact the undersigned attorney at (808) 523-8984, business hours Hawaii standard time, or via email at <sethreiss@lawhi.com>, in order that the undersigned attorney may endeavor to resolve any outstanding issues as expeditiously as possible thereby to avoid prolonged prosecution of the present application.

This paper is being mailed and faxed (without enclosures) within **four** months of the November 18, 2003 mailing date of the Office Action to which it responds. The number of independent claims and the total number of claims, after amendment, are within the number paid for with the filing fee. A Petition for Extension of Time Under 37 CFR § 1.136(a), Form PTO/SB/22 (12-04) requesting

a one month extension, and a $60 small entity fee for filing a response within one month of the applicable response deadline, is enclosed together with this amendment and response.

Respectfully submitted,

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